REMARKS

Status of Claims

In order to expedite prosecution, claims 1-49 have been cancelled without prejudice or disclaimer as to the claimed subject matter. Applicants respectfully reserve the right to pursue the subject matter of cancelled claims 1-49 in one or more continuation or divisional applications. Claims 50 and 55 are amended herein. Claims 50-62 will be pending on entry of the current amendments. Claim 61 stands withdrawn. It is understood that withdrawn subject matter will be rejoined upon allowance of a generic linking claim.

Support for the amended claims can be found throughout the specification as originally filed, *inter alia*, on page 14, lines 13-18, and on page 15, lines 3-5. Accordingly, applicant submits that no new matter is introduced into the specification by way of the present amendments. Accordingly, applicant respectfully requests entry of the amendments, and reconsideration of the remaining pending claims.

Information Disclosure Statement

Applicants would like to thank the examiner for considering the IDS of 12/19/2003 in part. The part of the IDS of 12/19/2003 not considered by the examiner is now provided in the IDS submitted with this Office Action to correct the typographical errors of the original IDS.

Priority

After entry of the above amendment to the specification, the first sentence of the specification references U.S. Application No. 10/375,906, to which the present application claims the benefit of priority under 35 U.S.C. § 121. Applicants believe that the present amendment addresses the examiner's objection and that the application is in compliance with 37 CFR 1.78(a). Applicants therefore respectfully request entry of the specification amendment and withdrawal of this objection to the specification.

Reply to Rejection Under 35 U.S.C. § 112, ¶ 1, Enablement

Claims 50-60 and 62 are rejected under 35 U.S.C. § 112, ¶ 1 as allegedly failing to comply with the enablement requirement.

Applicants respectfully disagree and traverse this rejection.

The Office Action, on page 10, makes the factually unsupported allegation that "the specification does not contain any guidance relating to a single metabolite that is useful in treating a disease that affects mammalian subjects." See Office Action at page 10, lines 1-3. Applicants respectfully disagree. Applicants submit that the specification offers guidance to those skilled in the art with regard to both specific compounds as well as specific diseases. For instance, the specification provides that intermediary metabolites, such as glycolipids recited in the present claims, may be used to treat diseases such as diseases including a defect in an immune response as part of the pathogenesis of the disease. Specifically, the specification provides as follows:

> Intermediary metabolites, such as glucosylceramides, can be used in accordance with this invention to treat various diseases, including cancer, infectious diseases and any immune-mediated pathogenic condition. For example in the instance of small cell carcinoma of the lung, subjects can be treated by administration of glucosylceramides such that at least one component of the immune system is elevated to such an extent that a specific activation of the NKT cell population is effected. Under these conditions the immune response to the cancer will be altered in such a manner that the cancer cells will be turned over or destroyed or lead to be destroyed and the subject will enter remission or experience a significant diminution of the cancer. A comparable effect can also be achieved by removing NKT cells from the subject and exposing these cells to glucosylceramides in vitro under conditions that will permit the survival and growth of the cells. When these ex vivo-trained cells are transferred back into the subject these cells will direct an immune response that can lead to a remission of the cancer or a significant diminution of the cancer.

See Specification at paragraph spanning pages 13 and 14.

Furthermore, at the top of page 15, the specification provides that glycolipids are useful in the current methods (see claim 50), and that specific glycolipids include monosaccharide ceramides (claim 55) and glucosyl ceramide and galatosyl ceramide (claim 56). Thus, the specification provides adequate teachings enabling one skilled in

the art to administer a glycolipid for the purposes of modulating at least one component of the immune system for the purposes of treating a disease that includes a defect in an immune response as part of the pathogenesis of the disease.

The Office Action at page 10 also makes the factually unsupported allegation that: "There is no information provided in the specification pertaining to the type of immune parameter that should be modulated to treat a disease." Again, Applicants respectfully disagree with this characterization. Applicants submit that immunoparameters or markers associated with particular immune diseases (such as those induced by viral infection, cancer and auto-immune diseases) are well known and established. Applicants further submit that a skilled artisan may use a particular immune parameter or marker to gauge whether a substance would be useful for the particular disease being investigated. The scope of the claims is amended herein to encompass diseases wherein the disease includes a defect in an immune response as part of the pathogenesis of the disease, and that the metabolite is a glycolipid. Applicants submit that these immune diseases (such as those induced by viral infection, cancer, and auto-immune diseases, for example) encompassed by the claims are a small portion of the "4000 different diseases" referenced in the Office Action. Applicants submit that a skilled artisan would understand the experimental results obtained, *i.e.*, changes in immunoparameters or markers, as evidence of a benefit for the treatment of the immune related disease under investigation.

Applicants submit that the specification provides evidence that specific immune parameters are modulated in response to a metabolite, such as a glycolipid. For example, Figures 1-6 illustrate the results of assays leading to T-cell proliferation and changes in IFNγ serum levels, IL-4 serum levels, and peripheral NKT lymphocytes. Additionally, the specification provides as follows:

> These assays and figures demonstrate that the presence of an increased level of a metabolite has led to significant changes in the immune profile of these subjects. Surprisingly, when this condition was accompanied by another immune system challenge (HCV infection), there was significant impact on the immune profile of the HCV+subjects compared to the subjects that lacked elevation of the metabolite.

See Specification at page 12, first full paragraph.

The specification therefore provides adequate teachings enabling one skilled in the art to administer a glycolipid for the purposes of modulating at least one immune parameter, such as IFNγ, for example. Applicant further submits that the working examples clearly set forth a protocol for testing an agents ability to modulate at least one component of the immune system, which amounts to adequate guidance to test a glycolipid of interest. Furthermore, a person of skill in the art is capable of associating changes in an immune marker or parameter with particular disease states. For instance, Matthys *et al.* (J Immunol. 1999 Sep 15;163(6):3503-10) teaches that in several models of autoimmune disease, including collagen-induced arthritis, endogenous IFNγ acts as a disease-limiting factor in the pathogenesis of the disease. Additionally, Takahashi *et al.* (Dig Dis Sci. 2006 Apr;51(4):677-86; Abstract) teaches that CD4+CD45RO+CD25+ T cell frequency was inversely correlated with the clinical and endoscopic severity of ulcerative colitis.

The Office Action at page 9 also alleges that: "The breadth of the claims encompasses a process for treatment of all diseases for all mammalian subjects by perturbing immunoparameters with the administration of any known metabolites." Applicants respectfully submit that the current amendments recite a method of treating a disease that includes a defect in an immune response as part of the pathogenesis of the disease. As such, the claims as currently amended more adequately define the subject matter sought and supported by the specification.

For the reasons above, Applicants respectfully submit that the instant specification provides sufficient information to enable a skilled artisan to make and use the invention commensurate with the scope of the presently amended claims without undue experimentation. Applicant respectfully requests reconsideration and withdrawal of this rejection.

Reply to Double Patenting Rejection

Claim 55 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 106 of copending application no. 10/675,980. Applicants respectfully submit that as this is a provisional double patenting rejection, no action is required by applicant until such time that the subject matter in copending application no. 10/675,980 is allowed. For the convenience of the examiner, applicants provide the relevant excerpt from M.P.E.P. 1504.06 Double Patenting, which states as follows:

> If a provisional double patenting rejection (of any type) is the only rejection remaining in two conflicting applications, the examiner should withdraw that rejection in one of the applications (e.g., the application with the earlier filing date) and permit the application to issue as a patent. The examiner should maintain the provisional double patenting rejection in the other application which rejection will be converted into a double patenting rejection when the first application issues as a patent. If more than two applications conflict with each other and one is allowed, the remaining applications should be cross rejected against the others as well as the allowed application.

In view of the foregoing, Applicants respectfully request the withdrawal of this and all other outstanding rejections and objections.

CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicant would appreciate the courtesy of a telephone call to their counsel to resolve such issues and place all claims in condition for allowance.

It is believed that no additional fees are required with this submission. However, in the event that additional fees are deemed necessary, or in the event of any variance between the amount enclosed and the fees determined by the USPTO, please charge or credit any such variance to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

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Dated: August 23, 2006 By: _____

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